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THE RELATIVE EFFECT OF PULSED RADIATION EXPOSURE IN PRODUCTION OF ACUTE MORTALITY IN MICE

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ADMINISTRATIVE INFORMATION

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ABSTRACT

Mice have been subjected to pulsed exposures of either fission spectrum neutrons or gamma radiation produced by a Triga Mark F reactor. The acute mortality response of animals given pulsed radiation of the order of 10^6 rads/min has been compared with mortality responses obtained by neutron irradiation at 40 rads/min and gamma irradiation at 100 rads/min. No significant differences in $LD_{50/30}$ were observed as a function of dose rate with either gamma or neutron irradiation.

SUMMARY

The Problem:

To determine the lethal effect of gamma and neutron radiation in mice at dose rates differing by several orders of magnitude. A comparison has been made between the radiation dose-response curves for CF#1 mice given pulsed radiation exposures of the order of 10^6 rads/min and animals exposed at rates of 100 rads/min or less. (The radiation source was a Triga Mark F reactor.)

The Findings:

No significant differences in $LD_{50/30}$ have been detected in neutron or gamma irradiated mice subjected to either burst exposure or exposure at more moderate radiation dose rates. In the neutron irradiation studies the comparison was made between pulsed (PP) dose rates of 0.4-1.0 x 10^6 rads/min and a rate of 40 rads/min achieved with sustained (SS) reactor operation (first collision doses); the $LD_{50/30}$ in both groups approximated 300 rads (midline tissue dose). Likewise, no difference in $LD_{50/30}$ was found in gamma irradiated animals exposed to PP dose rates of 0.9-4.0 x 10^6 rads/min and SS animals irradiated at 100 rads/min; in both groups the $LD_{50/30}$ approximated 790 rads.

INTRODUCTION

The relationship between radiation intensity and biological effect has been studied using various exposure techniques. These exposures range in time from chronic exposure over nearly the lifetime of animals to essentially instantaneous exposure lasting a few milliseconds (1-4). Very little is known, especially in mammalian systems, about the comparative biological consequences of short exposures, which involve intensities of the order of $0.4 - 4.0 \times 10^6$ rads/min. Biological experiments conducted in conjunction with detonations of nuclear weapons yield valuable information pertaining to high intensity irradiation, but these experiments are perturbed by the existence of various mixtures of radiations as well as by other factors which render the evaluation of such data difficult.

The purpose of the present experiment is to evaluate, under well controlled conditions, the relative potencies of pulsed radiation exposure as compared to radiation exposures of several minutes duration. Previous mouse-lethality experiments have been conducted with a pulsing reactor (5) but no comparative studies were undertaken; consequently, the desired comparative information is not available. The present report deals with the acute mortality responses of neutron and gamma irradiated mice.

MATERIAL AND METHODS

The radiation source in these experiments was a Triga Mark F reactor, the characteristics of which have been published in detail (6). In brief, extensive dosimetric studies using film, threshold detectors, and tissue equivalent ionization chambers have been conducted to characterize the neutron flux, tissue dose of gamma and neutron radiations as well as distribution of dose in a one inch mouse phantom. Each exposure was monitored by the use of either sulfur threshold detectors in the case of the neutron exposures. or phosphate glass dosimeters in the case of gamma exposures. These values were related to the tissue dose in each case. Dose rate estimates are based on first collision dose (in rads), and LD_{50} estimates are expressed as midline tissue dose (in rads). Details of the animal exposure facility, and a complete description of the radiation characteristics and dosimetry of the system have been reported (7). At the front surface of the phantom, the neutron/gamma ratio during neutron exposure was 6:1, and the gamma/neutron ratio during gamma exposure was 99:1. For neutron irradiation, mice were placed in 12 lusteroid tubes and were affixed to a specially designed mouse board to assure isodose exposure. This board was placed within a lucite cannister which was lowered 25 ft. inside an aluminum tube into the neutron beam. The exposure time for neutron irradiated animals varied as follows: with sustained reactor operation (SS) at a first collision dose rate of 40 rad/min, the exposure times were 7.5-11.4 minutes; in the pulsing operations (PP) the dose rates were $0.4\text{-}1.0 \times 10^6$ rad/min, with exposure times of 24-40 milliseconds.

In the pulsing situation, an inverse relationship exists between dose and exposure time; consequently, the dose rate increases as the dose is increased.

For gamma irradiation, mice were exposed in groups of 10 using the same devices as were used for neutron exposure. In SS operation the animals were exposed at a first collision dose rate of 100 rad/min with exposure times of 8.0-12.0 minutes; in PP operation the dose rates were $0.93 - 4.2 \times 10^6$ rad/min over a duration of 17-44 milliseconds.

The mice used in these experiments were CF#1 females, 3-4 months old, weighing 22-28 g. These experimental animals were selected on the basis of their freedom from pigment-producing pseudomonads as determined by standard bacteriological procedures performed on samples of drinking water. That this screening was effective is indicated by negligible mortality during the first post-irradiation week in the gamma irradiated mice.

RESULTS

Acute mortality response was the endpoint used for comparison of the effectiveness of pulsed (PP) and steady-state (SS) exposure to either neutron or gamma radiation. Median lethal doses and fiducial limits were calculated with an IBM 704 computer using a USNRDL program based on computations of Aitchison and Brown (8) and Finney (9).

The neutron radiation dose-response curves presented in Figure 1 indicate no significant difference in $LD_{50/30}$ between the SS and PP exposed animals. Also, no significant differences were detected in

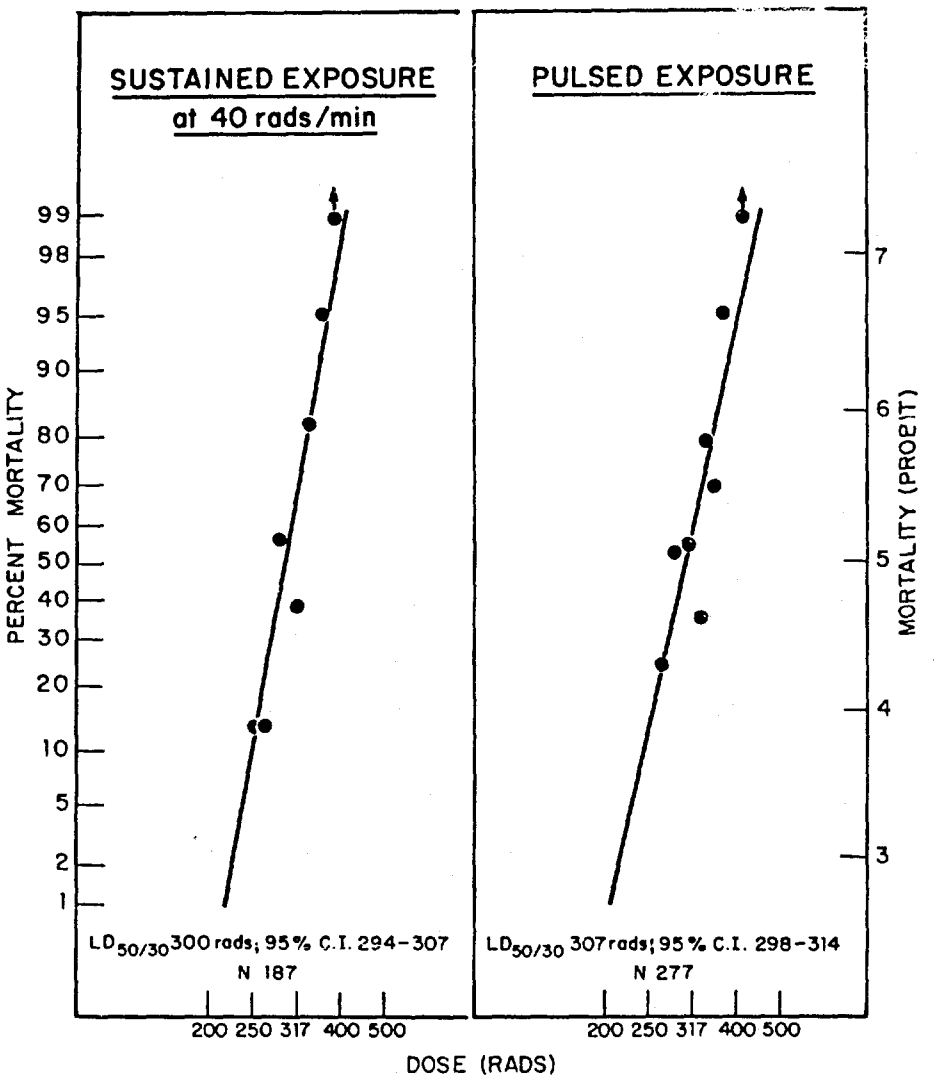

Fig. 1 Radiation dose response of neutron irradiated mice.

either mean survival times (M.S.T.) or slopes (b) of probit regression lines; these values are: SS, M.S.T. 8.91 ± 0.38 days and b, 7.39 ± 0.66; PP, M.S.T. 9.04 ± 0.28 days and b, 5.86 ± 0.56.

Likewise, gamma radiation dose-response curves shown in Figure 2 reveal no significant differences between PP and SS in $LD_{50/30}$, M.S.T., or b. For SS mice, the M.S.T. is 12.60 ± 0.31 days and b is 8.31 ± 1.03; in the PP group the M.S.T. is 12.79 ± 0.34 and b is 6.63 ± 0.99. The cumulative mortality curves for pooled (PP and SS) data (Fig. 3) show the well known difference in survival patterns between neutron and gamma irradiated mice; by 10 days, mortality was 73% and 29% respectively.

DISCUSSION

The effect of radiation dose rate on acute mortality responses in mammals has been extensively explored over an intensity range of less than one to several hundred roentgens per minute (2, 10), but heretofore, no comparative studies have been conducted involving intensities approximating 10^5 - 10^6 rad/min. A decreased effectiveness of high intensity radiation bursts has been reported in radiochemical (11) and some biological systems (3, 4, 12). However, over the dose ranges employed in the present study, no dose rate dependency of the acute mortality response has been detected for neutron or gamma irradiated mice.

Although previous data on exposure of mice to neutrons produced by cyclotron beams have required exposure times of several minutes (13), it is significant that these results are also in agreement with mortality data on mice exposed to reactor neutron beams. Since the cyclotron

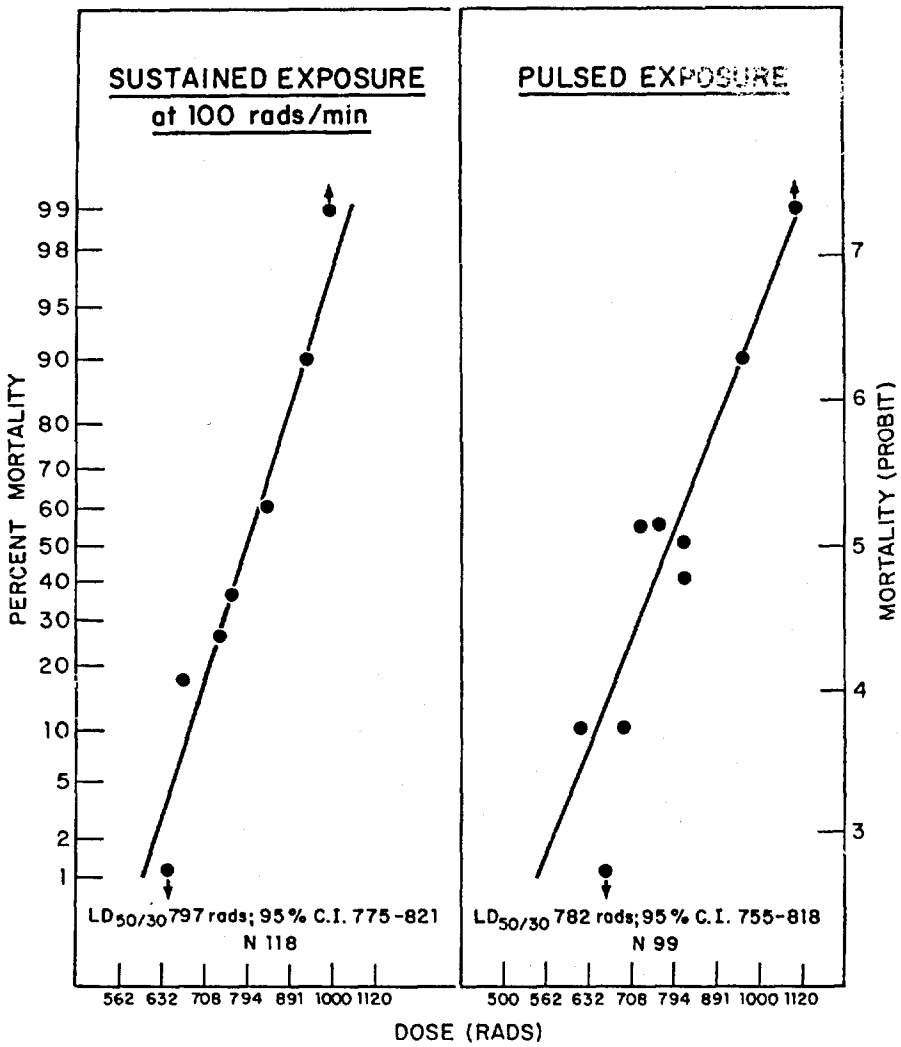

Fig. 2 Radiation dose response of gamma irradiated mice.

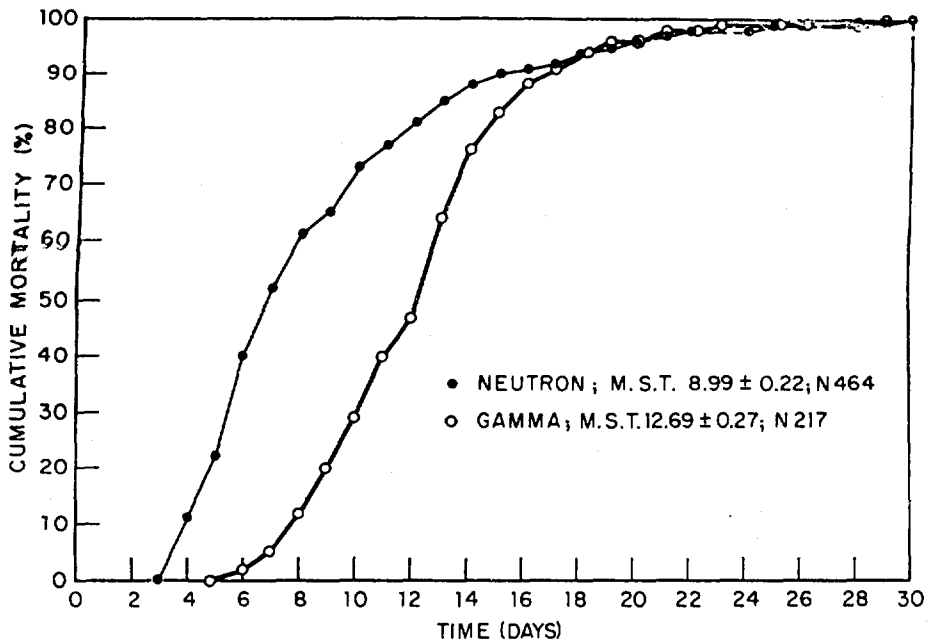

Fig. 3. Cumulative mortality of neutron and gamma irradiated mice.

is also a pulsed beam with pulse durations of only 10^{-8} - 10^{-9} seconds, instantaneous dose rates must have exceeded these reported by us here by at least several orders of magnitude. This suggests that radiation given in even much shorter time periods than the 10^{-2} seconds reported here is equally effective insofar as mortality is concerned.

These results imply that reversal or repair processes which may significantly alter the effectiveness of radiation and which are operative at much lower dose rates (2, 14) play no significant role during the exposure periods used in the present experiments. Also indicated is that recombination of free radicals, partial anaerobiosis, or other mechanisms advanced to account for decreased effectiveness of burst exposures (11, 12, 14) are likewise inoperative in terms of the acute mortality response for the dose rates used here.

Furthermore, in terms of the acute mortality response in mice, the present data indicate that results of experiments conducted at radiation dose rates in excess of 7-10 rad/min. are probably applicable to the prompt ionizing radiation situation encountered in a nuclear detonation.

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